

1. (original) A screening method for identifying a methoxyphosphonate nucleotide analogue prodrug conferring enhanced activity in a target tissue comprising:
  - (a) providing at least one of said prodrugs;
  - (b) selecting at least one therapeutic target tissue and at least one non-target tissue;
  - (c) administering the prodrug to the target tissue and to said at least one non-target tissue; and
  - (d) determining the relative activity conferred by the prodrug in the tissues in step (c).
2. (new) The method of claim 1 wherein the activity is antiviral activity or antitumor activity.
3. (new) The method of claim 2 wherein the activity is antiviral activity.
4. (new) The method of claim 3 wherein the activity is anti-HIV or anti-HBV activity.
5. (new) The method of claim 1 wherein the prodrug is a prodrug of PMPA or PMEA.
6. (new) The method of claim 5 wherein the prodrug is a phosphonoamidate, phosphonoester or mixed phosphonoamidate/phosphonoester.
7. (new) The method of claim 6 wherein the amide is an amino acid amide.
8. (new) The method of claim 6 wherein the ester is an aryl ester.
9. (new) The method of claim 1 further comprising selecting a prodrug having a relative activity in the target tissue that is greater than 10 times that of the non-target tissue.

10. (new) The method of claim 1 wherein the target and non-target tissue are in an animal, the prodrug is administered to the animal and the relative activity is determined by analysis of the animal tissues after administration of the prodrug.

11. (new) The method of claim 1 wherein activity in the target and non-target tissues is determined by assaying the amount of at least one metabolite of the prodrug in the tissues.

12. (new) The method of claim 12 wherein the metabolite is the parental drug.

13. (new) The method of claim 12 wherein the metabolite is the diphosphate of the parental drug.

14. (new) The method of claim 1 wherein the target tissue is virally infected tissue and the non-target tissue is the same tissue which is not virally infected.

15. (new) The method of claim 1 wherein the target tissue is lymphoid tissue and the activity is anti-HIV activity.

16. (new) The method of claim 1 wherein the target tissue is liver and the activity is anti-HBV activity.

17. (new) The method of claim 1 wherein the target tissue is hematological and the activity is antitumor activity.

18. (new) The method of claim 1 wherein the target tissue is malignant and the non-target tissue is the same tissue but non-malignant.